

57. (Amended) The modified CTLA4-immunoglobulin fusion protein of claim 56, wherein the first peptide comprises an extracellular domain of the CTLA4 protein.

- 58. (Amended) The modified CTLA4-immunoglobulin fusion protein of claim 57 wherein the first peptide comprises amino acid residues 1-125 of the human CTLA4 protein.
- 59. (Amended) The modified CTLA4-immunoglobulin fusion protein of claim 56, wherein the immunoglobulin constant region comprises a hinge region, a CH2 domain and a CH3 domain.
- 61. (Amended) A CTLA4-immunoglobulin fusion protein, comprising a first peptide having at least one CTLA4 activity and a second peptide comprising an immunoglobulin constant region wherein the immunoglobulin constant region comprises the CH1 domain, hinge region, CH2 domain, and CH3 domain from a Cy4 heavy chain.
- 62. The peptide of claim 61, wherein the immunoglobulin constant region is modified to reduce at least one constant region-mediated biological effector function.
- 63. (Amended) The peptide of claim 61, wherein the first peptide has at least one CTLA4 activity and the hinge region of the second peptide includes at least one cysteine residue available for disulfide bond formation.
- 65. (Amended) The CTLA4-immunoglobulin fusion protein of claim 59, wherein the CH2 domain is modified to reduce at least one biological effector function.
- 66. (Amended) The CTLA4-immunoglobulin fusion protein of claim 65, wherein the biological effector function is selected from the group consisting of complement activation and Fc receptor interaction.
- 67. (Amended) The CTLA4-immunoglobulin fusion protein of claim 66, wherein the CH2 domain is modified by substitution of an amino acid residue located at a position of an intact immunoglobulin heavy chain selected from the group consisting of position 234, position 235 and position 237.





69. (Amended) The CTLA4-immunoglobulin fusion protein of claim 67 comprising the amino acid sequence shown in SEQ ID NO: 28.

Please add new Claims 92-94 indicated below:

- --92. (New) The CTLA4-immunoglobulin protein of claim 69, wherein said fusion protein comprises a Leu to Glu substitution at position 235 and a Gly to Ala substitution at position 237.
- 93. (New) The CTLA4-immunoglobulin protein of claim 61, wherein said fusion protein comprises a Leu to Glu substitution at position 235 and a Gly to Ala substitution at position 237.
- 94. (New) The CTLA4-immunoglobulin protein of claim 67, wherein said fusion protein comprises a Leu to Glu substitution at position 235 and a Gly to Ala substitution at position 237.--

REMARKS

Claims 56-59, 61-63, 65-67, 69, and 92-94 are currently pending in the application. A Sequence Listing which complies with the requirements of 37 C.F.R. §1.821 is submitted herewith. The paper copy of the Sequence Listing is identical in substance to the material on this diskette previously submitted for the parent application 09/227,595. The computer readable form of the Sequence Listing previously submitted for the parent application 09/227,595 is understood to comply with the requirements of §1.824(d).

The Pending Claims are Enabled

It is Applicants position that the quantity of experimentation necessary to practice the claimed invention is not undue and that the experimentation amounts to no more than routine screening.

The Court of Appeals for the Federal Circuit in *In re Wands*, USPQ 2d 1400 (Fed. Cir. 1988) set forth the factors that should be considered when determining whether or not a required amount of